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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/582,850	06/14/2006	Bertram Cezanne	MERCK-3185	6766

23599 7590 05/27/2010

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EXAMINER	
JARRELL, NOBLE E	

ART UNIT	PAPER NUMBER
1624	

NOTIFICATION DATE	DELIVERY MODE
05/27/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@mwzb.com

Office Action Summary	Application No.	Applicant(s)	
	10/582,850	CEZANNE ET AL.	
	Examiner	Art Unit	
	NOBLE JARRELL	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,15-26,28,30-38,40 and 41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,15-20,22-26,28,30-38,40 and 41* is/are rejected.

7)☒ Claim(s) *21* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12 February 2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group XI in the reply filed on 12 February 2010 is acknowledged. The traversal is on the ground(s) that the restriction should be withdrawn. This is not found persuasive because doing a complete search on formula I of claim 1 is burdensome. Searching each possibility of a compound embraced by formula I requires multiple independent searches based on the meaning of variable T. It is noted that when variable T is piperidine, variable D can be a cyclic group (this search can be run). Consequently, this type of search was done.

The requirement is still deemed proper and is therefore made FINAL among groups where variable T is different.

Specification

2. The abstract of the disclosure is objected to because there is no ending period. Correction is required. See MPEP § 608.01(b).

Priority

3. The priority date of the instant application is 19 November 2004.

Information Disclosure Statement

4. The information disclosure statement filed 12 February 2010 has been acknowledged and considered.

Claim Objections

5. Claim 1 is objected to because of the following informalities: a species is listed after the genus of formula I. Appropriate correction is required. It is unclear why this compound is recited after the genus.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-13, 15-19, 22-26, 28, 30-38, 40, and 41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds in which variable D is phenyl, piperidine, quinoline, or 1-azabicyclo[2.2.2]octane and variable T is piperidine, phenyl, piperazine, morpholine, or cyclohexane , does not reasonably provide enablement for all compounds encompassed by the genus of formula I. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to compounds in which a piperidine ring is modified with a Q-cyclic group at its 4-position and a C(O)-CH(R^1)-(NR^3 or O)-C(O or S or NH or N-CN or N-NO_2)-ND-cyclic group at its one 1-position. Thus, the claims taken together with the specification imply that all compounds embraced by this genus can be prepared.

(3) The state of the prior art

The prior art (discussed below under the 35 U.S.C. 102 and 103 rejections) describes that compounds in which variable D is piperidine

(4) The predictability or unpredictability of the art:

The prior art (see references applied under 35 U.S.C. 102 and 103 rejection) teaches that compounds in which variable D is phenyl, quinoline, piperidine, or 1-azabicyclo[2.2.2]octane and variable T is piperidine, phenyl, piperazine, morpholine, or cyclohexane can be prepared.

(5) The relative skill of those in the art:

Those of relative skill in the art are those with level of skill of the authors of the references cited to support the examiner's position (MD's, PhD's, or those with advanced degrees and the requisite experience in preparation of compounds embraced by instant formula I).

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for guidance for compounds in which variable D is phenyl, piperidine, quinoline, or 1-azabicyclo[2.2.2]octane and variable T is piperidine, phenyl, piperazine, morpholine, or cyclohexane can be prepared.

However, the specification does not provide guidance for not all compounds encompassed by instant formula I.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to claims 1-13, 15-19, 22-26, 28, 30-38, 40, and 41 and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be

burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

8. Claims 23 and 24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the inhibition of thrombosis (through Factor VIIIa and Xa) and melanomas (through Factor VIIa), does not reasonably provide enablement for alleviation of all cancers. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to inhibition of Factor VIIa or Xa with a compound in which a piperidine ring is modified with a Q-piperidine substituent and cyclic group-NH-C(O, S, or N)-NR^3/O-CH(R^1)-C(O) group. Thus, the claims taken together with the specification imply that a compound embraced by formula I can inhibit a disease mediated by inhibition of Factor VIIa or Xa.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

Turpie (*Expert Opinion on Pharmacotherapy*, **2004**, *5(6)*, 1373-84) describes that Factor Xa inhibition leads to antithrombotic therapy.

Hembrough et al. (*Cancer Research*, **2003**, *63*, 2997-3000) describes that less Factor VIIa inhibitor is required in antithrombotic therapy than in alleviation of melanoma (page 2998, paragraph 1, and page 3000, paragraph 2).

Cancer is more than 100 different diseases ("Cancer definition", http://www.medterms.com/script/main/art.asp?articlekey=2580, accessed 27 November 2007).

(5) The relative skill of those in the art:

Those of relative skill in the art are those with level of skill of the authors of the references cited to support the examiner's position (relative skill of those in this art is MD's, PhD's, or those with advanced degrees and the requisite experience in the inhibition of factor Xa or VIIa in a patient).

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for alleviation of a melanoma and thrombosis in a patient.

However, the specification does not provide guidance for alleviation of the broad spectrum of cancers.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to claims 23 and 24 and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-5, 7-13, 15, 16, 22-26, 28, 38, 40, and 41 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In these claims, the $C(R^2)_n$ (where variable n is zero, one or two) group has an unfulfilled octet for the carbon atom where n is zero or one. What substituents do applicants intend to be present when n is zero or one? Do applicants mean to say $-[C(R^2)_2]_{n-}$? The intended meaning is not clear in the claims.

11. Claims 13, 18, 19, and 20 recite that variable X can be NR^3. There is insufficient antecedent basis for this limitation in the claim because variable R^3 is not recited in claim 1. In claim 1, variable R^3 exists.

Claim Rejections - 35 USC § 102

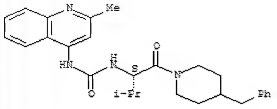
12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1, 4, 5, 6, 9, 10, 12, 13, 15, 16, 22, 25, 26, and 28 are rejected under 35 U.S.C. 102(a) as being anticipated by Aissaoui et al. (WO 2003048154, published 12 June 2003, IPC C07D401/12). Aissaoui describes compound 239 (page 20, shown below). In this compound, the following definitions are applied: D is 2-methyl-4-quinolinyl; Y is O; X is NH; R^1 is isopropyl; Q is methylene; and T is phenyl.

RN 1064717-66-3 ZCAPLUS
CN Urea, N-[(1S)-2-methyl-1-[[4-(phenylmethyl)-1-piperidinyl]carbonyl]propyl]-N'-(2-methyl-4-quinolinyl)- (CA INDEX NAME)

Absolute stereochemistry.

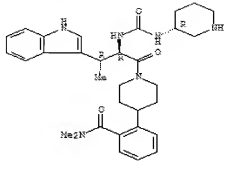


Pharmaceutical compositions are described (page 26, line 19 to page 27, line 30). Methods of use are described (page 25, line 2 to page 26, line 18). Scheme B (page 30) describes a synthesis that encompasses claim 22.

14. Claims 1, 6, 12, 13, 16, 22, 25, 26, and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen et al. (US 5721251, issued 24 February 1998). Chen describes compounds (example 107, column 168, lines 45-67, Registry number 203941-64-4, and salts thereof; example 113, column 172, lines 1-23, Registry number 203941-73-5). Each of these compounds is shown below. In these compounds, D is 3-piperidinyl or 1-azabicyclo[2.2.2]oct-3-yl, Y is O, X is NH, R^1 is CH(Me)-1*H*-indol-3-yl, Q is a bond, and T is 2-C(O)NMe_e-phenyl ring.

RN 203941-64-4 ZCAPLUS
CN Benzamide, 2-[1-[(2R,3R)-3-(1H-indol-3-yl)-1-oxo-2-[[[(3R)-3-piperidinylamino]carbonyl]amino]butyl]-4-piperidinyl]-N,N-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.

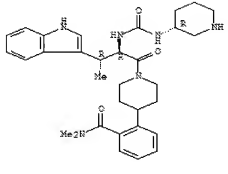


RN 203941-65-5 ZCAPLUS
CN Benzamide, 2-[1-[(2R,3R)-3-(1H-indol-3-yl)-1-oxo-2-[[[(3R)-3-piperidinylamino]carbonyl]amino]butyl]-4-piperidinyl]-N,N-dimethyl-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 203941-64-4
CMF C32 H42 N6 O2

Absolute stereochemistry.

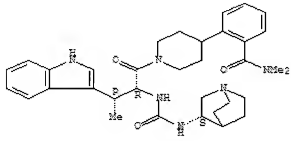


CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 203941-73-5 ZCAPLUS
CN Benzamide, 2-[1-[(2R,3R)-2-[[[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]carbonyl]amino]-3-(1H-indol-3-yl)-1-oxobutyl]-4-piperidinyl]-N,N-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.

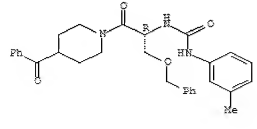


Pharmaceutical compositions comprising these compounds are described (abstract; column 48, lines 7 to 52; column 50, line 48 to column 51, line 35). The utility of these compounds is described (column 47, line 22-57; column 48, lines 53 to column 50, line 47).

15. Claims 1, 2, 4, 5, 12, 13, 15, 16, and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Holladay et al. (*Bioorganic and Medicinal Chemistry Letters*, **1995**, *5(24)*, 3057-62). Holladay describes compounds 19, 21, 23, 12, 13, 15, 16, 17, 20, and 22 (each on page 3059), 33, 32 (page 3060), and 8 and 9 (page 3058). These compounds are shown below.

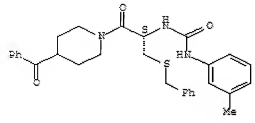
RN 162881-40-5 ZCAPLUS
CN Piperidine, 4-benzoyl-1-[2-[[[(3-methylphenyl)amino]carbonyl]amino]-1-oxo-3-(phenylmethoxy)propyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



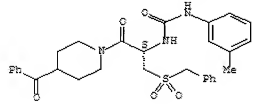
RN 162881-49-4 ZCAPLUS
CN Piperidine, 4-benzoyl-1-[2-[[[(3-methylphenyl)amino]carbonyl]amino]-1-oxo-3-[(phenylmethyl)thio]propyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



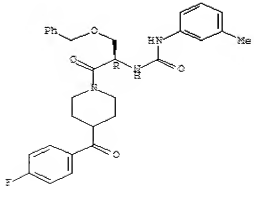
RN 162881-50-7 ZCAPLUS
CN Piperidine, 4-benzoyl-1-[2-[[[(3-methylphenyl)amino]carbonyl]amino]-1-oxo-3-[(phenylmethyl)sulfonyl]propyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



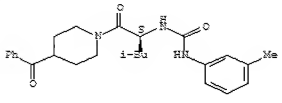
RN 162881-52-9 ZCAPLUS
CN Piperidine, 4-(4-fluorobenzoyl)-1-[2-[[[(3-methylphenyl)amino]carbonyl]amino]-1-oxo-3-(phenylmethoxy)propyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



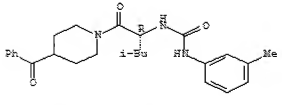
RN 173986-89-5 ZCAPLUS
CN Piperidine, 4-benzoyl-1-[4-methyl-2-[[[(3-methylphenyl)amino]carbonyl]amino]-1-oxopentyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



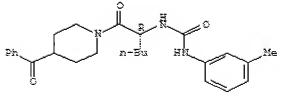
RN 173986-90-8 ZCAPLUS
CN Piperidine, 4-benzoyl-1-[4-methyl-2-[[[(3-methylphenyl)amino]carbonyl]amino]-1-oxopentyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



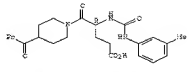
RN 173986-92-0 ZCAPLUS
CN Piperidine, 4-benzoyl-1-[2-[[[(3-methylphenyl)amino]carbonyl]amino]-1-oxohexyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



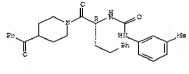
RN 179586-53-1 REGISTRY
CN 1-Piperidinepentanoic acid, 4-benzoyl-γ-[[(3-methylphenyl)amino]carbonyl]amino]-δ-oxo-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



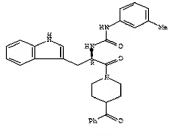
RN 179586-54-2 REGISTRY
CN Piperazine, 4-benzoyl-1-[2-[[(3-methylphenyl)amino]carbonyl]amino]-1-oxo-4-phenylbutyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



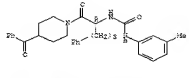
RN 179586-56-3 REGISTRY
CN Piperazine, 4-benzoyl-1-[3-(1H-indol-3-yl)-2-[[(3-methylphenyl)amino]carbonyl]amino]-1-oxopropyl]-, (2)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



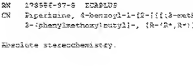
RN 179586-96-4 REGISTRY
CN Piperazine, 4-benzoyl-1-[2-[[(3-methylphenyl)amino]carbonyl]amino]-1-oxo-5-phenylpentyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



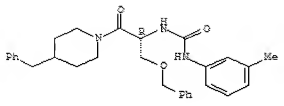
RN 179586-57-5 REGISTRY
CN Piperazine, 4-benzoyl-1-[2-[[(3-methylphenyl)amino]carbonyl]amino]-1-oxo-3-(phenylmethoxy)butyl]-, (R-(R*,R*))- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



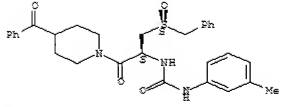
RN 173987-02-5 ZCAPLUS
CN Piperidine, 1-[2-[[[(3-methylphenyl)amino]carbonyl]amino]-1-oxo-3-(phenylmethoxy)propyl]-4-(phenylmethyl)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



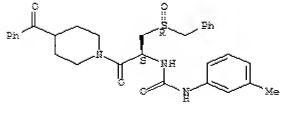
RN 174172-92-0 ZCAPLUS
CN Piperidine, 4-benzoyl-1-[2-[[[(3-methylphenyl)amino]carbonyl]amino]-1-oxo-3-[(phenylmethyl)sulfinyl]propyl]-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 174172-93-1 ZCAPLUS
CN Piperidine, 4-benzoyl-1-[2-[[[(3-methylphenyl)amino]carbonyl]amino]-1-oxo-3-[(phenylmethyl)sulfinyl]propyl]-, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

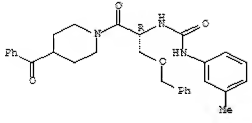


16. Claims 1, 2, 4, 5, 12, 13, 16, and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Kerwin et al. (US 5346907, issued 13 September 1994). Kerwin describes compounds (column 8, lines 59-60 and 66-67; column 9, lines 1-4 and 7-14) in which the following definitions apply: variable D is 3-

methyl-phenyl, unsubstituted phenyl, 3-methoxy-phenyl, 3-chlorophenyl, Y is O, X is NH, R^1 is methylene-O-benzyl, Q is C(O), and T is unsubstituted phenyl or 4-fluorophenyl. Each of these compounds is shown below.

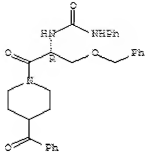
RN 162881-40-6 ZCAPLUS
CN Piperidine, 4-benzoyl-1-[2-[[[(3-methylphenyl)amino]carbonyl]amino]-1-oxo-3-(phenylmethoxy)propyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



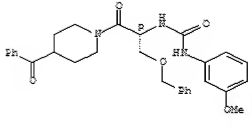
RN 162881-45-0 ZCAPLUS
CN Piperidine, 4-benzoyl-1-[1-oxo-2-[[(phenylamino)carbonyl]amino]-3-(phenylmethoxy)propyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



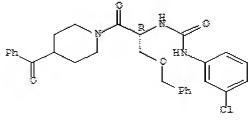
RN 162881-46-1 ZCAPLUS
CN Piperidine, 4-benzoyl-1-[2-[[[(3-methoxyphenyl)amino]carbonyl]amino]-1-oxo-3-(phenylmethoxy)propyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



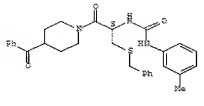
RN 162881-47-2 ZCAPLUS
CN Piperidine, 4-benzoyl-1-[2-[[[(3-chlorophenyl)amino]carbonyl]amino]-1-oxo-3-(phenylmethoxy)propyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



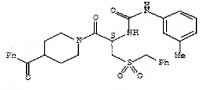
RN 162881-49-4 ZCAPLUS
CN Piperidine, 4-benzoyl-1-[2-[[[(3-methylphenyl)amino]carbonyl]amino]-1-oxo-3-[(phenylmethyl)thio]propyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



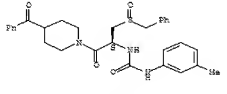
RN 162881-50-7 ZCAPLUS
CN Piperidine, 4-benzoyl-1-[2-[[[(3-methylphenyl)amino]carbonyl]amino]-1-oxo-3-[(phenylmethyl)sulfonyl]propyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



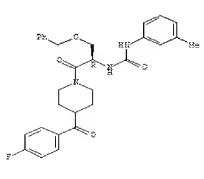
RN 162881-51-8 ZCAPLUS
CN Piperidine, 4-benzoyl-1-[2-[[[(3-methylphenyl)amino]carbonyl]amino]-1-oxo-3-[(phenylmethyl)sulfinyl]propyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 162881-52-9 ZCAPLUS
CN Piperidine, 4-[4-fluorobenzoyl)-1-[2-[[[(3-methylphenyl)amino]carbonyl]amino]-1-oxo-3-(phenylmethoxy)propyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



Pharmaceutical compositions are described (column 76, line 6 to column 77, line 17). These compounds antagonize cholecystokinin and gastrin (column 1, lines 17-26) and are administered to mice *in vivo* (80 µg/ kg s.c.) (column 73, line 10 to column 75, line 7).

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

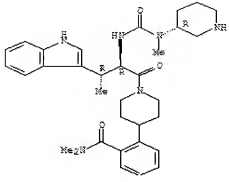
19. Claims 1, 6, 12, 13, 16, 22, 25, 26, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (US 5721251, issued 24 February 1998).

Determining the scope and contents of the prior art

Chen describes compounds (column 26, lines 15-30, Registry number 203941-69-9; example 110, column 170, lines 1-67, Registry number 203941-70-2). Each of these compounds is shown below. In these compounds, D is 3-piperidinyl, Y is O, X is NH, R^1 is CH(Me)-1*H*-indol-3-yl, Q is a bond, and T is 2-C(O)NMe_2-phenyl ring. These compounds are shown below

RN 203941-69-9 ZCAPLUS
CN Benzamide, 2-[1-[(2R,3R)-3-(1H-indol-3-yl)-2-[[[methyl(3R)-3-piperidinylamino]carbonyl]amino]-1-oxobutyl]-4-piperidinyl]-N,N-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.

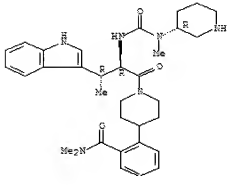


RN 203941-70-2 ZCAPLUS
CN Benzamide, 2-[1-[(2R,3R)-3-(1H-indol-3-yl)-2-[[[methyl(3R)-3-piperidinylamino]carbonyl]amino]-1-oxobutyl]-4-piperidinyl]-N,N-dimethyl-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 203941-69-9
CMF C33 H44 N6 O3

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

Pharmaceutical compositions comprising these compounds are described (abstract; column 48, lines 7 to 52; column 50, line 48 to column 51, line 35). The utility of these compounds is described (column 47, line 22-57; column 48, lines 53 to column 50, line 47).

Ascertaining the differences between the prior art and the claims at issue

In instant claim 1, variable D is attached to an NH group. Chen describes compound in which variable D is attached to an N-Me group.

Resolving the level of ordinary skill in the pertinent art

Those of relative skill in the art are those with level of skill of the authors of the references cited to support the examiner's position (MD's, PhD's, or those with advanced degrees and the requisite experience in preparation of compounds of instant formula I).

Considering objective evidence present in the application indicating obviousness or nonobviousness

Sterling Drug Inc. v. Watson, Comr. Pats. (108 USPQ 37) teaches that the test to be applied in the matter of the patentability of a compound that is a homologue of another is that the beneficial characteristics are both unexpected and obvious."

In the application of *Sterling* to the instant application, equivalency is taught between H and Me (the difference examples 107 and 110 is NH-D (in example 107) versus N(Me)-D (in example 110). Since these compounds have therapeutic use (growth hormone promoters), sufficient motivation exists to prepare these compounds exists.

Allowable Subject Matter

20. Claim 21 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

21. Claims 21 is not anticipated or rendered obvious by the prior art of record because none of the references describe a compound in which Q is a halogen-substituted-phenyl ring and T is a piperidinyl, piperazinyl, or morpholine ring.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NOBLE JARRELL whose telephone number is (571)272-9077. The examiner can normally be reached on M-F 7:30 A.M - 6:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Noble Jarrell/
Examiner, Art Unit 1624